

SIMPLE PREDICTORS TO DIFFERENTIATE ACUTE RESPIRATORY INFECTIONS FROM ACUTE ASTHMA IN CHILDREN 6 MONTHS TO 5 YEARS

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CERTIFICATE

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DECLARATION

I declare that this dissertation entitled " **SIMPLE PREDICTORS TO DIFFERENTIATE ACUTE RESPIRATORY INFECTIONS FROM ACUTE ASTHMA IN CHILDREN 6 MONTHS TO 5 YEARS** " has been conducted by me at the Institute of Child Health and Hospital for Children, under the guidance and supervision of my unit ex-chief **Prof. Dr. Mallika Pathmanaban, MD, DCH**, and **Prof. Dr. P. Venkataraman MD, DCH**. It is submitted in part of fulfillment of the award of the degree of M.D. (Pediatrics) for the March 2008 examination to be held under The Tamil Nadu Dr.M.G.R Medical University, Chennai. This has not been submitted previously by me for the award of any degree or diploma from any other university.

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INTRODUCTION

Acute respiratory infections constitute one of the principal causes of morbidity and mortality in children less than five years of age in developing countries. It is estimated that 3.9 million children die annually from ARI, most of them been from developing countries^{1,2}. Pneumonia, refers to an infection of the lungs, which can be caused by a variety of microorganisms, including viruses, bacteria, fungi, and parasites.

Signs and symptoms

Symptoms of pneumonia vary, depending on the age of the child and the cause of pneumonia. Some common symptoms include:

Fever

Chills

Cough

Unusually rapid breathing

Breathing with grunting or wheezing sounds

Labored breathing that makes a child's rib muscles retract

Vomiting

Chest pain

Abdominal pain

Decreased activity

Loss of appetite (in older children) or poor feeding (in infants)

In extreme cases, cyanosis.

When pneumonia is caused by bacteria, the child usually becomes sick relatively quickly and experiences the sudden onset of high fever and unusually rapid breathing. When pneumonia is caused by viruses, symptoms tend to appear more gradually and are often less severe than in bacterial pneumonia. Wheezing may be more common in viral pneumonia. In developing countries, like India, with high infant mortality rates, pneumonia is contributed mainly by bacteria. Agents causing pneumonia are far wide when compared to adult population.

Pathophysiology of pneumonia:³

Viral pneumonia

Viruses reach the lungs when airborne droplets are inhaled through the mouth and nose. Once in the lungs, the virus invades the cells lining the airways and alveoli. This invasion often leads to cell death, either when the virus directly kills the cells, or through a type of cell self-destruction called apoptosis. When the immune system responds to the viral infection, even more lung damage occurs. White blood cells, mainly lymphocytes, activate certain chemical cytokines which allow fluid to leak into the alveoli. This combination of cell destruction and fluid-filled alveoli interrupts the normal transportation of oxygen into the bloodstream. In addition to damaging the lungs, many viruses affect other organs and thus disrupt many body functions. Viruses can also make the body more susceptible to bacterial infections; bacterial pneumonia often complicates viral pneumonia. Viral pneumonia is commonly caused by viruses such as influenza virus, respiratory syncytial virus (RSV), adenovirus, and metapneumovirus. Herpes simplex virus is a rare cause of pneumonia except in newborns. Those with a

compromised immune system are also at risk of pneumonia caused by cytomegalovirus (CMV).

Bacterial pneumonia

Bacteria typically enter the lung when airborne droplets are inhaled, but can also reach the lung through the bloodstream, when there is an infection in another part of the body. Many bacteria live in parts of the **upper respiratory tract**, such as the nose, mouth and sinuses, and can easily be inhaled into the alveoli. Once inside, bacteria may invade the spaces between cells and between alveoli through connecting pores. This invasion triggers the **immune system** to recruit **neutrophils**. The neutrophils **engulf** and kill the offending organisms, and also release **cytokines**, causing a generalised activation of the immune system. This leads to the fever, chills and fatigue, common in bacterial and fungal pneumonia. The neutrophils, bacteria, and fluid from surrounding blood vessels fill the alveoli and interrupt normal oxygen transportation.

Bacteria often travel from an infected lung into the bloodstream, causing serious or even fatal illness such as septic shock with low blood pressure and damage to multiple organs including the brain, kidneys, and heart. Bacteria can also travel to the area between the lungs and the chest wall (the pleural cavity) causing a complication called empyema.

The most common causes of bacterial pneumonia are *Streptococcus pneumoniae*, other Gram-positive bacteria and ‘atypical’ bacteria. The types of Gram-positive

bacteria that cause pneumonia can be found in the nose or mouth of many healthy people. *Streptococcus pneumoniae*, often called "pneumococcus", is the most common bacterial cause of pneumonia in all age groups except newborn infants. Another important Gram-positive cause of pneumonia is *Staphylococcus aureus*. Gram-negative bacteria cause pneumonia less frequently than gram-positive bacteria. Some of the Gram-negative bacteria that cause pneumonia include *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Moraxella catarrhalis*. These bacteria often live in the stomach or intestines and may enter the lungs if vomitus is inhaled. 'Atypical' bacteria which cause pneumonia include *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae*, and *Legionella pneumophila*.

Common causes of pneumonia

Newborns : Group B Streptococcus (GBS), respiratory syncytial virus (RSV).

Infants

Viruses : Parainfluenza viruses, influenza virus, adenovirus, and respiratory syncytial virus (RSV), cytomegalovirus.

Atypical organisms : *Chlamydia trachomatis*, *Ureaplasma urealyticum*, and *Pneumocystis carinii* (PCP).

Bacteria : *B. pertussis*, *Streptococcus pneumoniae*,
Haemophilus influenzae, *Mycobacterium tuberculosis*.

Young children

Viruses : Parainfluenza viruses, influenza virus,
adenovirus and respiratory syncytial virus

Atypical organisms: *Mycoplasma pneumoniae*.

Bacterial: Pneumococcus, *Mycobacterium tuberculosis*.

Older children and adolescents:

Atypical organisms: *Mycoplasma pneumoniae*, *Chlamydia trachomatis*.

Bacterial: Pneumococcus, *B. pertussis*, *Mycobacterium tuberculosis*.

Types of pneumonia

Community-acquired pneumonia: Community-acquired pneumonia (CAP) is infectious pneumonia in a person who has not recently been hospitalized. CAP is the most common type of pneumonia. The most common causes of CAP differ depending on a person's age, but they include *Streptococcus pneumoniae*, viruses, the atypical bacteria, and *Haemophilus influenzae*. Overall, *Streptococcus pneumoniae* is the most common cause of community-acquired pneumonia worldwide.

Hospital-acquired pneumonia: Hospital-acquired pneumonia, also called nosocomial pneumonia, is pneumonia acquired during or after hospitalization for another illness or procedure with onset at least 72 hrs after admission. The causes, microbiology, treatment and prognosis are different from those of community-acquired pneumonia. Up to 5% of patients admitted to a hospital for other causes subsequently develop pneumonia. Hospitalized patients may have many risk factors for pneumonia, including mechanical ventilation, prolonged malnutrition, underlying heart and lung diseases, decreased amounts of stomach acid, and immune disturbances. Additionally, the microorganisms a person is exposed to in a hospital are often different from those at home . Hospital-acquired microorganisms may include resistant bacteria such as MRSA, *Pseudomonas*, *Enterobacter*, and *Serratia*. Ventilator-associated pneumonia (VAP) is a subset of hospital-acquired pneumonia. VAP is pneumonia which occurs after at least 48 hours of intubation and mechanical ventilation.

Other types of pneumonia

- Severe acute respiratory syndrome (SARS)

SARS is a highly contagious and deadly type of pneumonia which first occurred in 2002 after initial outbreaks in China. SARS is caused by the SARS coronavirus, a previously unknown pathogen. New cases of SARS have not been seen since June 2003.

- Bronchiolitis obliterans organizing pneumonia (BOOP)

BOOP is caused by inflammation of the small airways of the lungs. It is also known as cryptogenic organizing pneumonitis (COP).

- Eosinophilic pneumonia

Eosinophilic pneumonia is invasion of the lung by eosinophils. Eosinophilic pneumonia often occurs in response to infection with a parasite or after exposure to certain types of environmental factors.

- Chemical pneumonia

Chemical pneumonia (usually called chemical pneumonitis) is caused by chemical toxins such as pesticides, which may enter the body by inhalation or by skin contact. When the toxic substance is an oil, the pneumonia may be called lipid pneumonia.

- Aspiration pneumonia

Aspiration pneumonia (or aspiration pneumonitis) is caused by aspirating foreign objects which are usually oral or gastric contents, either while eating, or after reflux or vomiting which results in bronchopneumonia. The resulting lung inflammation is not an infection but can contribute to one, since the material aspirated may contain anaerobic bacteria or other unusual causes of pneumonia. Aspiration is a leading cause of death among hospital and nursing home patients, since they often cannot adequately protect their airways and may have otherwise impaired defenses.

Diagnosis of pneumonia

Complete blood count: WBC count is often increased with a polymorphic predominance in bacterial infections^{4,5}. Lymphocytic predominance may be seen in viral pneumonias, pertussis and atypical infections.

Cultures: In the cooperative older child with a productive cough, a sputum Gram stain is useful. Sputum cultures and immunofluorescent antibody testing may be useful.

Bactec cultures (sputum or blood) are useful to isolate the organisms.

Imaging Studies: Chest x-ray PA view is the diagnostic test for pneumonias. Sometimes to differentiate from a syn-pneumonic effusion, a USG chest may be required. In rare cases of children who have an effusion or an empyema identified on CXR, a CT scan may be needed to further define the scope of the problem.

Mantoux test: To diagnose pneumonia due to mycobacterial tuberculosis.

Cold agglutinin test: A bedside cold agglutinin test may help confirm the clinical suspicion of mycoplasmal infection. This test is performed by placing a small amount of blood in a specimen tube containing anticoagulant and inserting this into a cup filled with ice water. After a few minutes in the cold water, the tube is held up to the light, tilted slightly, and slowly rotated. Small clumps of red blood cells coating the tube are indicative of a positive test result. This test is positive only in about one half of the cases of mycoplasmal infection and has high chances of false positive reactions.

Other tests: If there is presence of pleural fluid, pleural fluid aspiration and culture and microscopy.

Etiological diagnosis of pneumonia is very difficult in young children because sputum is not readily available. Rapid diagnostic procedures like counter immune electrophoresis, Elisa, latex agglutination have a very low sensitivity. Only culture of lung aspirates and blood cultures will provide an etiological diagnosis. Ideal management in treating pneumonia is by rapidly establishing etiological diagnosis and prescribing antimicrobials. However clinical, laboratory and radiological features do not

reliably distinguish between bacterial and viral cause. Segmental and lobar consolidation is even caused by viruses though pathognomonic for bacterial etiology. Diffuse infiltrates are also caused by bacteria though more commonly caused by viruses. Total count, differential count, CRP, ESR do not reliably distinguish between bacterial and viral etiology. The Gold standard for establishing etiological diagnosis is only by way of culture of lung aspirates which is practically impossible in developing countries. So, even in developed countries, etiological diagnosis of pneumonia is established only in less than one-fourth. This calls for empirical treatment of pneumonia with antimicrobials

Treatment of pneumonia:

Oxygen is required if there is grunting, flaring, severe tachypnoea, and retractions.

Bacterial Pneumonia: Antibiotics: oral or intravenous

Penicillins: They are appropriate first-line agents in children in whom pneumococcal disease is strongly suspected^{6,7}. They have limited activity against gram-negative bacteria due to resistance.

- Amoxicillin: 40 mg/kg/day PO divided tid/ 100 mg/kg/day IV tid
- Penicillin V: 40 mg/kg/d PO divided qid
- Crystalline Penicillin: 1,00,000 units/kg/day IV in 6 divided doses.
- Ampicillin/sulbactam: 40mg/kg/day PO divided tid, 100 mg/kg/day IV qid
- Amoxicillin/clavulanic acid: 40mg/kg/d PO divided tid, 100 mg/kg/d IV tid

Cephalosporins: First generation cephalosporins: They are useful against Gram positive organisms and *Proteus mirabilis*, *H influenzae*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Moraxella catarrhalis*.

- Cephalexin: 50 mg/kg/day PO bid
- Cefadur : 30-50 mg/kg/day PO bid.
- Cefuroxime: 30 mg/kg/d PO bid, IV: 150-200 mg/kg/d IV tid.
- Cefalothin: 50 mg/kg/day PO qid / 100 mg/kg/day IV qid.

Second generation cephalosporin: They are useful against Gram positive organisms and have limited activity against Gram negative organisms.

- Cefaclor: 20-40 mg/kg/day PO tid.

Third generation cephalosporins: They are broad-spectrum antibiotics having good Gram-negative activity.

- Cefixime: 8 mg/kg/day PO bid.
- Ceftriaxone: 50-100 mg/kg/d IV/IM bd not to exceed 1 g.
- Cefotaxime: 100-200 mg/kg/d IV/IM divided q6-8h.
- Cefpodoxime: 10 mg/kg/d PO divided bid
- Cefprozil: 30 mg/kg/d PO divided bid

Chloramphenicol: It is a bacteriostatic drug having good Gram positive and Gram negative coverage. It is given along with penicillin and is especially useful in patients with *H. influenza* infections. Dose: 100mg/kg/day IV/IM.

Cotrimoxazole : 21 mg/kg/day PO/IV for 21 days. Useful for PCP pneumonia.

Macrolides: They are used for treatment of staphylococcal and streptococcal infections. Also used in the treatment of atypical pneumonias due to mycoplasma, chlamydia.

- Erythromycin: 30-50 mg/kg/d PO divided q6-8h.
- Clarithromycin: 15 mg/kg/d PO divided q12h.
- Azithromycin: Day 1: 10 mg/kg PO once; not to exceed 500 mg/d Days 2-5: 5 mg/kg PO qd; not to exceed 250 mg/d.

Vancomycin is used in children with penicillin resistant streptococci and methicillin resistant staphylococci. Dose: 45-50 mg/kg/day IV qds

Viral pneumonia

- RSV: Serious infections with this organism usually occur in infants with underlying lung disease. Aerosolized ribavirin can be given to severely affected infants.
- Herpes virus: Acyclovir is available for treatment of these pneumonias. Dose: 10 mg/kg/dose IV q8h; infuse over 1 h
- Influenza A pneumonia, which is particularly severe or when it occurs in a high-risk patient, may be treated with amantadine.
- Children who are toxic: Antibiotic therapy should include vancomycin

(particularly in areas where penicillin resistant streptococci have been identified) and a cephalosporin.

Integrated Management of Neonatal and Childhood Illnesses

WHO/UNICEF have developed a new approach for tackling the major diseases of early childhood called the Integrated Management of Childhood Illnesses⁸(IMCI). Studies show that children presenting with any illness often suffer from more than one disease. For instance, a child presenting with diarrhoea may also be malnourished and may not have received the immunization as per the National Immunization schedule. The integrated approach ensures that all relevant needs of the child are looked at and attended to, during the contact of the child with the health workers.

The IMNCI package has been developed by experts including the Child Health Researchers, academicians, the Indian Academy of Pediatrics (IAP) and the National Neonatology Forum (NNF) to adapt it for the specific requirements of children in India. Since newborn care is an important issue for bringing down the infant mortality rate in India, this aspect has been included in the package adapted by India. This package includes the following interventions ⁸:

Care of Newborns and Young Infants (infants under 2 months)

- Keeping the child warm.
- Initiation of breastfeeding immediately after birth and counseling for exclusive breastfeeding and non-use of pre lacteal feeds.

- Cord, skin and eye care.
- Recognition of illness in newborn and management and/or referral.
- Immunization
- Home visits in the postnatal period.

Home visits are an integral part of this intervention. Home visits by health workers (ANMs, AWWs, ASHAs and link volunteers) help mothers and families to understand and provide essential newborn care at home and detect and manage newborns with special needs due to low birth weight or sickness.

Three home visits are to be provided to every newborn starting with first visit on the day of birth (day 1) followed by visits on day 3 and day 7. For low birth weight babies, 3 more visits (total of six visits) are to be undertaken before the baby is one month of age. The details of these visits are given in the training package.

In addition, the opportunity of home visit is to be used for the care of mothers during the post-partum period. This will help mothers and families on how to recognize and manage minor conditions and will ensure timely referral of severe cases.

Care of Infants (2 months to 5 years)

- Management of diarrhoea, acute respiratory infections (pneumonia) malaria, measles, acute ear infection, malnutrition and anemia.

- Recognition of illness and at risk conditions and management/referral)
- Prevention and management of Iron and Vitamin A deficiency.
- Counseling on feeding for all children below 2 years
- Counseling on feeding for malnourished children between 2 to 5 years.
- Immunization

After neonatal period, IMNCI package is accessed by the family for their newborns/children from the health workers in the community (ANM, AWW, ASHA or link volunteer) or providers at the facility (PHC/CHC/FRU).

The current WHO strategy for control of mortality due to ARI relies heavily on STANDARDISED CASE MANAGEMENT^{9,10}. This includes utilization of simple signs and symptoms with high sensitivity and specificity to be adopted at first level health facilities by paramedics. Thus among children with ARI four main groups have been identified.

- Very severe disease
- Severe pneumonia.
- Pneumonia
- No pneumonia

CLASSIFICATION OF ILLNESS

Very severe disease:

Signs:

- Abnormally sleepy or difficult to wake
- Stridor
- Severe malnutrition
- Not able to drink
- Convulsions

Treatment:

- Refer URGENTLY to hospital
- Give first dose of antibiotic
- Treat fever
- Treat wheeze if audible

Severe pneumonia:

Signs:

- Chest indrawing:
- Grunt
- Cyanosis

Treatment:

- Refer URGENTLY to hospital
- Give first dose of antibiotic

Pneumonia:

Signs:

- ♦ No chest indrawing
- ♦ Fast breathing

2-12 months: Respiratory rate \geq 50/min

12-59 months: Respiratory rate $\geq 40/\text{min}$

Treatment:

- Give antibiotic
- Home care
- Review after two days or if getting worse

No pneumonia:

Signs:

- No chest indrawing
- No fast breathing

Treatment:

- Home care
- Treat fever and wheeze if present

The major clinical guidelines for the diagnosis of pneumonia pertain to fast breathing and other features of respiratory distress like chest indrawing, central cyanosis or inability to drink. An identical clinical presentation may occur in several other potentially fatal conditions that necessitate different therapeutic modalities. These include acute exacerbation of asthma, congestive cardiac failure, metabolic acidosis and raised intracranial pressure.

At the time of conception of these simple guidelines in the early 1980s, pneumonia could have been the predominant condition with this clinical presentation. However, it is possible that with the passage of time, the epidemiology of various

conditions presenting with fast breathing and other features of respiratory distress may have considerably altered.

Amongst the above mentioned other causes of rapid breathing, there is now enough data globally to prove that the prevalence and severity of asthma is increasing in all age groups ^{11,12,13,14}. In this context, it is also important to appreciate that asthma related fatalities do occur and can be largely prevented by an accurate diagnosis and early institution of appropriate therapy including broncho-dilators ^{15,16}.

For logistic reasons, the WHO recommended case management is structured towards treatment as pneumonia in preference to acute asthma. It is warned that wheezing can occur during pneumonia and therefore, care must be taken when treating wheezing not to miss treating pneumonia with an antibiotic ^{17,18}. Further, the need for bronchodilator therapy is guided by the presence of a wheeze which for paramedical personnel pertains to only an estimated one-third episodes in which the wheeze may be audible without the aid of a stethoscope. Thus, according to the current guidelines, in a child with cough and rapid breathing, there is a predilection for over-treatment for pneumonia with antibiotics and for under-treatment for asthma with bronchodilators. There is thus an urgent need for refining the available algorithm for case management to reliably differentiate pneumonia from acute asthma¹⁹.

ASTHMA

Asthma is a chronic inflammatory disorder of the airways characterized by an obstruction of airflow, which may be completely or partially reversed with or without

specific therapy²⁰. Airway inflammation is the result of interactions between various cells, cellular elements, and cytokines. In susceptible individuals, airway inflammation may cause recurrent or persistent bronchospasm, which causes symptoms including wheezing, breathlessness, chest tightness, and cough, particularly at night or after exercise. Approximately 500,000 annual hospitalizations (34.6% in persons ≤ 18 y) are because of asthma. The cost of illness related to asthma is around \$6.2 billion. Each year, an estimated 1.81 million people (47.8%) require treatment in the emergency department. Among children and adolescents aged 5-17 years, asthma accounts for a loss of 10 million school days and costs caretakers \$726.1 million because of work absence. Globally, morbidity and mortality associated with asthma have increased over the last 2 decades. This increase is attributed to increasing urbanization. Despite advancements in our understanding of asthma and the development of new therapeutic strategies, the morbidity and mortality rates due to asthma definitely increased between 1980 and 1995. In most children, asthma develops before they are aged 5 years, and, in more than half, asthma develops before they are aged 3 years. Among infants, 20% have wheezing with only upper respiratory tract infections (URTIs), and 60% no longer have wheezing when they are aged 6 years. Many of these children were called ‘transient wheezers’. They tend to have no allergies, although their lung function is often abnormal. These findings have led to the idea that they have small lungs. Children in whom wheezing begins early, in conjunction with allergies, are more likely to have wheezing when they are aged 6 and 11 years. Similarly, children in whom wheezing begins after they are aged 6 years often have allergies, and the wheezing is more likely to continue when they are aged 11 years.

Symptoms and signs:

- Cough
- Fast breathing
- Retractions
- Decreased activity
- Grunt and wheeze (audible and auscultatory)
- Cyanosis, in extreme cases.

Pathophysiology: Interactions between environmental and genetic factors result in airway inflammation, which limits airflow and leads to functional and structural changes in the airways in the form of bronchospasm, mucosal edema, and mucus plugs.

Airway obstruction causes increased resistance to airflow and decreased expiratory flow rates. These changes lead to a decreased ability to expel air and may result in hyperinflation. The resulting overdistention helps maintain airway patency, thereby improving expiratory flow; however, it also alters pulmonary mechanics and increases the work of breathing.

Hyperinflation compensates for the airflow obstruction, but this compensation is limited when the tidal volume approaches the volume of the pulmonary dead space; the result is alveolar hypoventilation. Uneven changes in airflow resistance, the resulting uneven distribution of air, and alterations in circulation from increased intraalveolar pressure due to hyperinflation all lead to ventilation-perfusion mismatch. Hypoxic vasoconstriction also contributes to this mismatch.

In the early stages, when ventilation-perfusion mismatch results in hypoxia, hypercarbia is prevented by the ready diffusion of carbon dioxide across alveolar capillary membranes. Thus, asthmatic patients who are in the early stages of an acute episode have hypoxemia in the absence of carbon dioxide retention. Hyperventilation triggered by the hypoxic drive also causes a decrease in PaCO₂. An increase in alveolar ventilation in the early stages of an acute exacerbation prevents hypercarbia. With worsening obstruction and increasing ventilation-perfusion mismatch, carbon dioxide retention occurs. In the early stages of an acute episode, respiratory alkalosis results from hyperventilation. Later, the increased work of breathing, increased oxygen consumption, and increased cardiac output result in metabolic acidosis. Respiratory failure leads to respiratory acidosis.

Chronic inflammation of the airways is associated with increased bronchial hyper-responsiveness, which leads to bronchospasm and typical symptoms of wheezing, shortness of breath, and coughing after exposure to allergens, environmental irritants, viruses, cold air, or exercise. In some patients with chronic asthma, airflow limitation may be only partially reversible because of airway remodeling (hypertrophy and hyperplasia of smooth muscle, subepithelial fibrosis) that occurs with chronic untreated disease.

New insights in the pathogenesis of asthma suggest the role of lymphocytes. Airway inflammation in asthma may represent a loss of normal balance between two "opposing" populations of Th lymphocytes. Two types of Th lymphocytes have been characterized: Th1 and Th2. Th1 cells produce IL-2 and IFN- γ , which are critical in

cellular defense mechanisms in response to infection. Th2, in contrast, generates a family of cytokines (IL-4, -5, -6, -9, and -13) that can mediate allergic inflammation. The current "hygiene hypothesis"²¹ of asthma illustrates how this cytokine imbalance may explain some of the dramatic increases in asthma prevalence in Westernized countries. This hypothesis is based on the assumption that the immune system of the newborn is skewed toward Th2 cytokine generation. Following birth, environmental stimuli such as infections will activate Th1 responses and bring the Th1/Th2 relationship to an appropriate balance.

Evidence exists that the prevalence of asthma is reduced in association with certain infections (*Mycobacterium tuberculosis*, measles, or hepatitis A); exposure to other children (eg, presence of older siblings and early enrollment in childcare); and less frequent use of antibiotics. Furthermore, the absence of these lifestyle events is associated with the persistence of a Th2 cytokine pattern.

Under these conditions, the genetic background of the child, with a cytokine imbalance toward Th2, will set the stage to promote the production of IgE antibody to key environmental antigens (e.g., dust mites, cockroaches, *Alternaria*, and possibly cats). Therefore, a gene-by-environment interaction occurs in which the susceptible host is exposed to environmental factors that are capable of generating IgE, and sensitization occurs. A reciprocal interaction seems to exist between the two subpopulations in which Th1 cytokines can inhibit Th2 generation and vice versa. Allergic inflammation may be the result of an excessive expression of Th2 cytokines. Alternately, the possibility that

the loss of normal immune balance arises from a cytokine dysregulation in which Th1 activity in asthma is diminished has been suggested in recent studies.

CLASSIFICATION OF CHRONIC ASTHMA:

The severity of asthma is classified as:

- mild intermittent
- mild persistent
- moderate persistent
- severe persistent

according to the frequency and severity of symptoms, including nocturnal symptoms, characteristics of acute episodes, and pulmonary function.

Mild intermittent disease

- Symptoms fewer than 2 times a week,
- Pulmonary function is normal between exacerbations.
- Exacerbations are brief, lasting from a few hours to a few days
- Nighttime symptoms occur less than twice a month.
- The variation in peak expiratory flow (PEF) is less than 20%.

Mild persistent asthma

- Symptoms more than 2 times a week but less than once a day.
- Exacerbations may affect activity.
- Nighttime symptoms occur more than twice a month..
- Pulmonary function test results demonstrate that the forced expiratory volume in 1 second (FEV1) or PEF is less than 80% of the predicted value, and the variation in PEF is 20-30%.

Moderate persistent asthma

- Daily symptoms, use inhaled short-acting beta2-agonists every day.
- Acute exacerbations in patients- more than 2 times a week and last for day
- The exacerbations affect activity.
- Nocturnal symptoms occur more than once a week.
- FEV1 and PEF values are 60-80% of the predicted values

- PEF varies by more than 30%.

Severe persistent asthma

- Continuous or frequent symptoms.
- Limited physical activity.
- Frequent nocturnal symptoms.
- FEV1 and PEF are less than 60% of the predicted values.
- PEF varies by more than 30%.

Since signs and symptoms of asthma and pneumonia have considerable overlap, in current WHO ARI CASE MANAGEMENT guidelines, in a child presenting with cough and rapid breathing, there is a predilection for over -treatment of pneumonia and under treatment of asthma.

LITERATURE REVIEW

Sachdev H.P.S et al conducted a case control comparison among children of acute asthma (n=100) and ARI (n=100), in 1995 in an urban referral centre- New Delhi. Only 34% of asthmatics had an audible wheeze. Significant independent predictors on multiple logistic regression analysis were number of earlier similar attacks and fever (or temperature). The best predictors for asthma were two or more earlier similar episodes (sensitivity 84%, specificity 84%) followed by temperature $< 37.6^{\circ}\text{C}$ (sensitivity 73% and specificity 84%). Absence of fever, audible wheeze and a family history of asthma had excellent specificity (98-100%) but low sensitivity (20-34%). It is concluded that simple clinical predictors can differentiate acute asthma and ARI. The recommended case management can, therefore, be refined by either: (i) Prescribing bronchodilators and no antibiotics with two or more earlier similar episodes of cough and rapid breathing; or (ii) To further minimize under treatment for pneumonia, prescribing bronchodilators as above, but denying antibiotics in such cases only if there is audible wheeze or family history of asthma or no fever²².

Sachdev H.P.S., in the year 2001, conducted a study in New Delhi, in 200 children presenting with acute onset of cough and respiratory distress. Those children in whom there was a previous similar episode were challenged with bronchodilator nebulisation. Their response to bronchodilator was then evaluated. Acute asthma was the predominant condition (46% or 54%), pneumonia alone was rare (10%), co-existence of pneumonia with wheeze (bronchospasm) was more frequent (22% or 15%) and often diagnoses not related to the respiratory system were documented (18% or 17%). All the

subjects in whom a preceding history of cough was not elicited had non-respiratory illnesses. An audible wheeze was appreciated in only 44 of the 150 cases (29.3%) with an auscultable wheeze. Conclusion: It is feasible to amalgamate simple clinical features (history of: (i) previous similar episode of cough and difficult breathing, and (ii) fever) in the WHO case management algorithm to significantly refine the antibiotic (95% CI range 7% to 33%) and bronchodilator (35%; 95% CI 27% to 43%) prescription²³. .

A multicentric study conducted in Pakistan by Hazir T et al on 1622 children aged between 6 months to 5 years, who presented with cough and respiratory distress with either auscultatory or audible wheeze were given 3 cycles of bronchodilator. The response of tachypnoea to bronchodilator was then evaluated. Result: Among 1004 children who were classified as having non severe pneumonia according to WHO classification, 621(61.8%) responded to bronchodilator. 383 children who were classified as severe pneumonia based on WHO classification, 145(38.14%) responded to bronchodilator²⁴.

A study was conducted by AV Castro et al in Brazil, in the year 2005, on 182 children, presenting with cough and tachypnoea. Each child had a chest X-ray that was read by two blinded, independent radiologists. Discordance between the two radiologists led to excluding 17 patients. The remaining 165 children were examined for fever and/or chest indrawing, and if they had a history of previous respiratory distress, challenged with a bronchodilator (BD). The association of persistent tachypnoea after BD and presence of pulmonary infiltrates was recorded. Results: The median age was 22 months

(mean 25.1 ± 14.5 mo) and 75.8% were aged ≥ 1 year. There were 58.8% males. Previous respiratory distress occurred in 65.0% and 79.2% of children aged <1 year and ≥ 1 year, respectively. Pneumonia was radiologically diagnosed in 26/165 (15.8%). 2/40 (5%) of children without a history of previous respiratory distress had pneumonia diagnosed. Of 125 children with history of previous respiratory distress, pneumonia was identified in 24 (19.2%). Persistence of tachypnoea after BD was associated with pulmonary infiltrate in 14/24 (58.3%), whereas, tachypnoea persisted in 32/101 (31.7%) children without pulmonary infiltrates ($P = 0.02$). The negative predictive value of resolution of tachypnoea was 87.3% (95% CI 77.5-93.4). BD non-response was most useful in children without fever and/or with chest indrawing to indicate pneumonia as the cause of the tachypnoea. This study indicates that by adding the simple procedures of a history of previous respiratory distress, recording of fever and chest indrawing, and observing the response to bronchodilators, pneumonia can be reliably identified in children presenting with tachypnoea and cough. It is probable that this approach to management of children with cough and tachypnoea could reduce unnecessary use of antibiotics. Negative predictive value for resolution of tachypnoea-87.3%²⁵.

In a multicentric study in Thailand in the year 2004, 521 children with wheeze were screened, 256 (49.1%) had WHO defined non-severe and 265 (50.9%) severe pneumonia. Wheeze was audible in only 48 (9.2%) of children. Of 256 non-severe pneumonia children, 217 (84.8%) responded to up to three cycles of bronchodilator. Of 265 severe pneumonia children, 189 (71.3%) responded. Among responders, 14 (6.4%) children in non-severe and 24 (12.7%) in the severe pneumonia group showed subsequent deterioration on follow-ups. A body temperature more than 100°F (37.7°C)

and severe pneumonia were identified as independent predictors of subsequent deterioration²⁶.

A study was conducted by Okoromah CN et al in Lagos to find out the rates of diagnosis and treatment of asthma among private practitioners. Relevant information on 45 asthmatic children was collected using pre-tested questionnaires. There were 30 (66.7%) males and 15 (33.3%) females (M:F, 2:1). Mean age, average ages for onset of symptoms and diagnosis of asthma were 9.4 years, 1.8 years and 6.6 years respectively. An average of 4 previous medical consultations were undertaken for asthma symptoms, but only 11 (24.4%) cases were labeled as asthma. Alternative diagnostic labels including allergy, bronchitis (wheezy), pneumonia (chest infection), and tuberculosis, were used in 29 (64.4%). Five (11.1%) cases were unlabelled. Alternative labeling for asthma was associated with frequent usage of non-bronchodilator medications including antihistamines, antibiotics, antituberculous drugs, cough mixtures, and herbal concoctions. Only 15 (33.3%) cases received bronchodilators, rarely prescribed regularly in the absence of asthma label. This study reveals low diagnosis and treatment rates for asthma, emphasising the need to audit the management of childhood asthma among medical practitioners, with the view of providing information²⁷.

STUDY JUSTIFICATION

According to WHO ARI CASE MANAGEMENT² guidelines, any child presenting with cough and rapid breathing, is indicative of pneumonia and the empirical treatment with antibiotics is suggested presuming bacterial etiology.

It is important to consider that asthma does occur in children presenting with

cough and fast breathing which can be treated with only bronchodilators¹⁵.

The various studies conducted all over the world^{22,23,24,25,26} also emphasise that the current WHO guidelines for ARI management leads to over treatment of pneumonia and under treatment of asthma. The present study was designed to find out the “Predictors” that can reliably distinguish acute pneumonia from asthma in children 6 months to 5 years. This will also reduce the unnecessary antibiotic use and enable timely use of bronchodilators.

OBJECTIVES OF THE STUDY

To study the value of

- Fever, chest indrawing and the response of tachypnoea to bronchodilator individually and in combination in predicting pneumonia among children aged 6 months to 5 years attending urban referral center.
- H/O previous similar episodes, H/O prior nebulisations, family H/O asthma in predicting asthma

SUBJECTS AND METHODS

Study design: Descriptive study

Study place: Out patient department

Study period: 2005-2007

Study population:

Inclusion criteria:

Children (6 months-5years) presenting with

- H/O acute cough,
- Respiratory distress,
- Fever

Exclusion criteria:

- ♦ Severe malnutrition,
- ♦ foreign body inhalation,
- ♦ chronic illness,
- ♦ H/O prior treatment with antibiotics ,
- ♦ grunt,
- ♦ stridor,
- ♦ cyanosis,
- ♦ unstable vitals,
- ♦ known asthmatic

Sample size: 245

Prevalence of ARI is 20%

Power was 80%,and

Alpha was 5%,

So the sample size calculated is,

$$n = z^2 P(1-P)/d^2$$

$$= 245$$

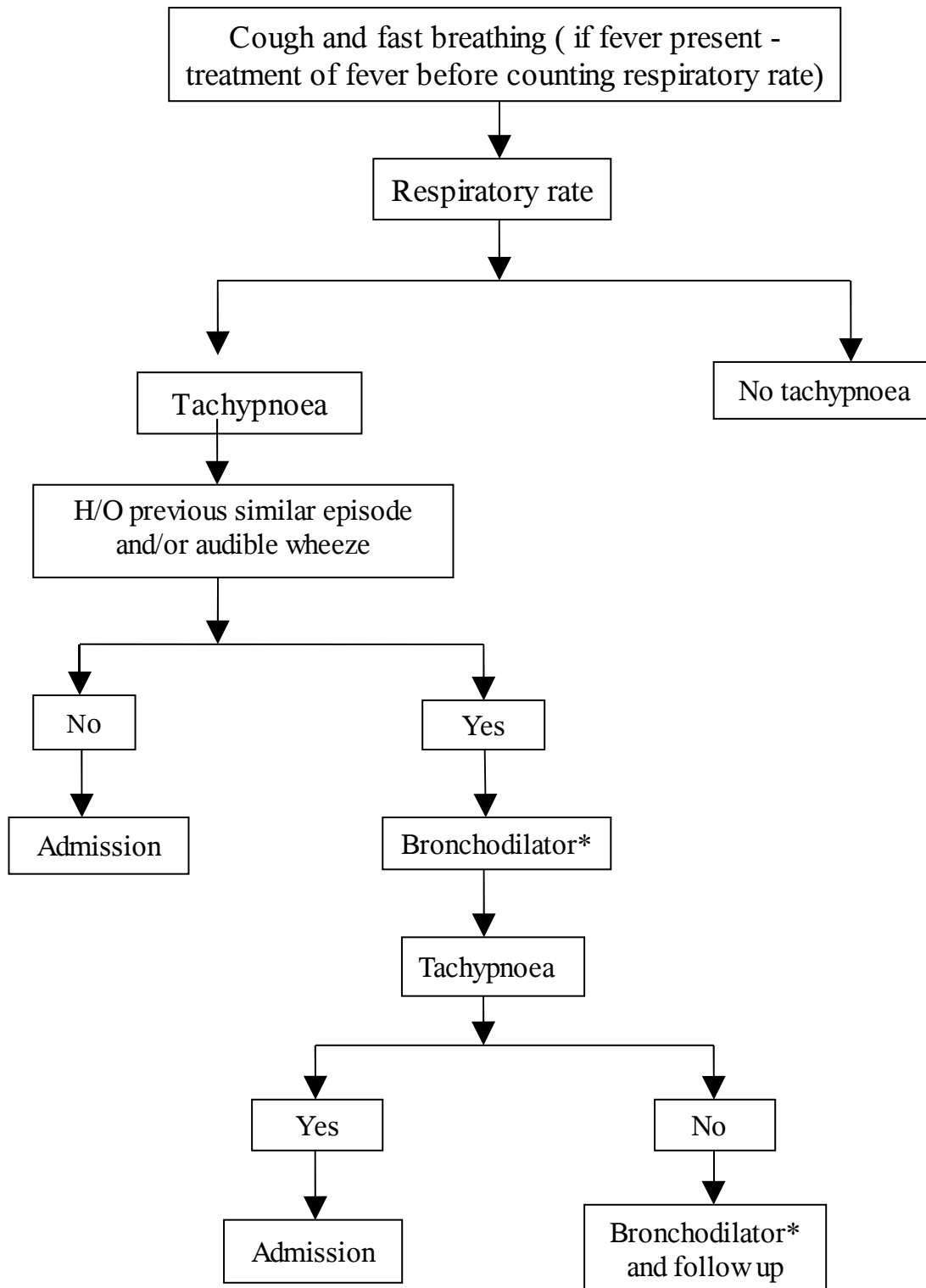
n= sample size

$$z=1.96,$$

$$\text{Precision (d)}=0.05,$$

$$\text{Prevalence (P)}=0.20$$

Manoeuvre: Figure A : Flow paths of cases in the study:



*Bronchodilator: 3 doses of beta2 agonist 0.1mg/kg/dose, each 20 minutes.

Diagnostic Definitions

Clinical diagnosis of pneumonia was made before reading the chest *X*-ray, if the respiratory frequency had not reduced under the cutoff limit for respective age stratum after three nebulisations.

Only Radiological diagnosis of pneumonia confirmed by two radiologists was considered as Gold standard. Agreement on interpretation of infiltrates between two pediatric radiologists was necessary for evaluation in the study.

The radiologists were not given clinical information and considered only three radiological patterns: (i) normal, (ii) presence of pulmonary infiltrates (reduced pulmonary view), or (iii) pulmonary hyperinflation without pulmonary infiltrate, based on WHO standards and definitions applied for epidemiological studies²⁸.

Bronchospasm was diagnosed if there was wheeze, absence of pulmonary infiltration on chest *X*-ray and rapid improvement (reduction of respiratory rate below cutoff limit for each age) after bronchodilator therapy.

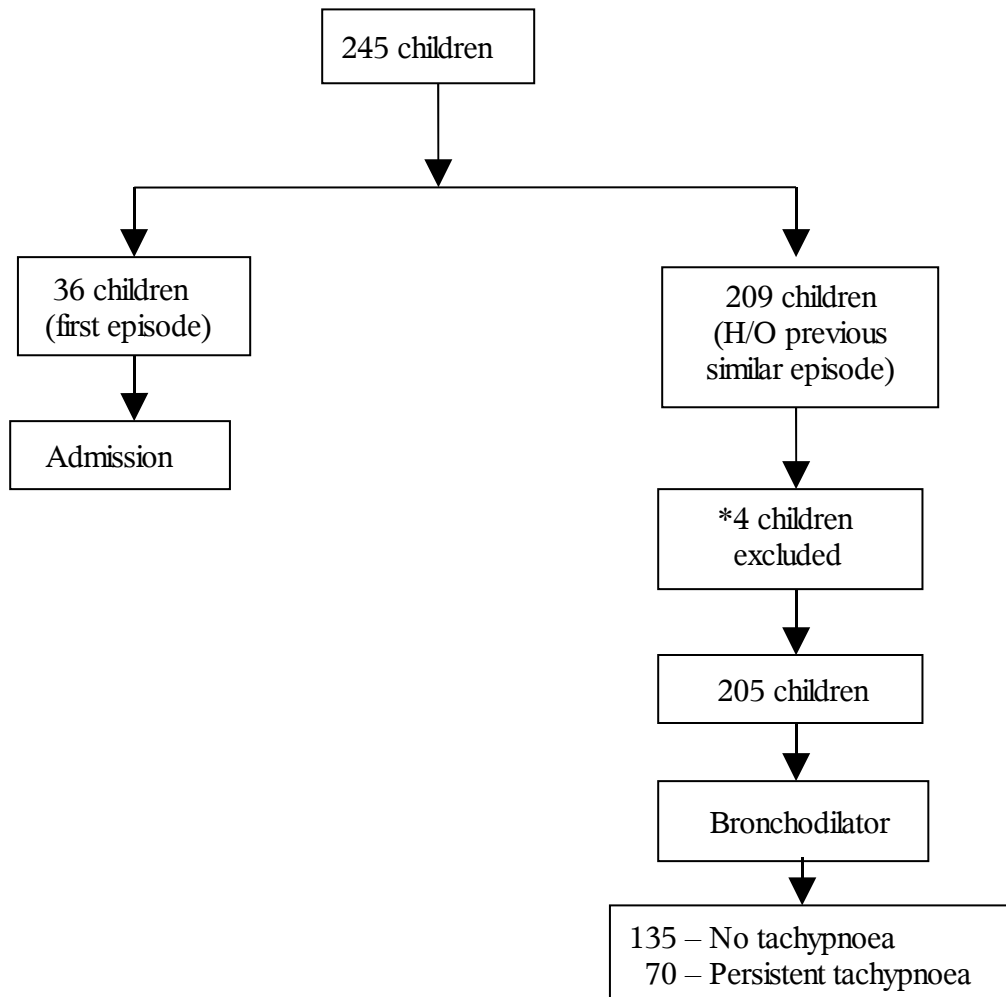
Co-existence of bronchospasm and pneumonia was defined if the respiratory rate decreased and there was concomitant pulmonary infiltrate on *X*-ray.

STATISTICAL ANALYSIS

Proportions of the children who had persistent tachypnoea following bronchodilator therapy and those in whom tachypnoea resolved were arrived at. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of the persistent tachypnoea following bronchodilator therapy, fever, chest indrawing in predicting pneumonia (infiltrates in the chest X ray) individually and in combination were arrived at among the entire study population. The same analysis was applied after excluding those children who had more than two previous similar episodes, family H/O asthma or allergy, previous nebulisations either alone or in combination, presence of these would point more towards asthma as the cause of cough and fast breathing. $P < 0.05$ was considered to be statistically significant.

RESULTS

Total No. of children in the study : 245



* 4

excluded due to discordance in chest x ray

Particulars of children who were excluded from the study

Sex	Response to bronchodilator	CXR Radiologist 1	CXR Radiologist 2
Female	Settled	Normal	Bronchopneumonia
Female	Not settled	BHI	Retrocardiac pneumonitis
Male	Not Settled	Normal	Bronchopneumonia with obstructive emphysema
Female	Not settled	Normal	Mild cardiomegaly

Table 1: First episode of respiratory distress (n=36)

Pneumonia	Male		Female		Total
	n	%	n	%	
Yes	12	50.0	10	27.7	22
No	10	27.7	4	11.1	14

Table 2: Symptoms and History analysis of 36 children

Symptoms + History	No. of children (n)	Percentage (%)
Fever	25	69.44
Cough + cold	36	100
Fast breathing	36	100
Chest indrawing	24	66.66
Decreased feed intake	27	75
Lethargy	27	75
Running nose	26	72.22
Vomiting	19	52.77
Audible wheeze	13	36.12
Cyanosis	0	0
Family H/O allergy /asthma	0	0
Previous H/O nebulisations	1	2.77

Previous similar episode	0	0
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Fig 1: Symptoms and history analysis

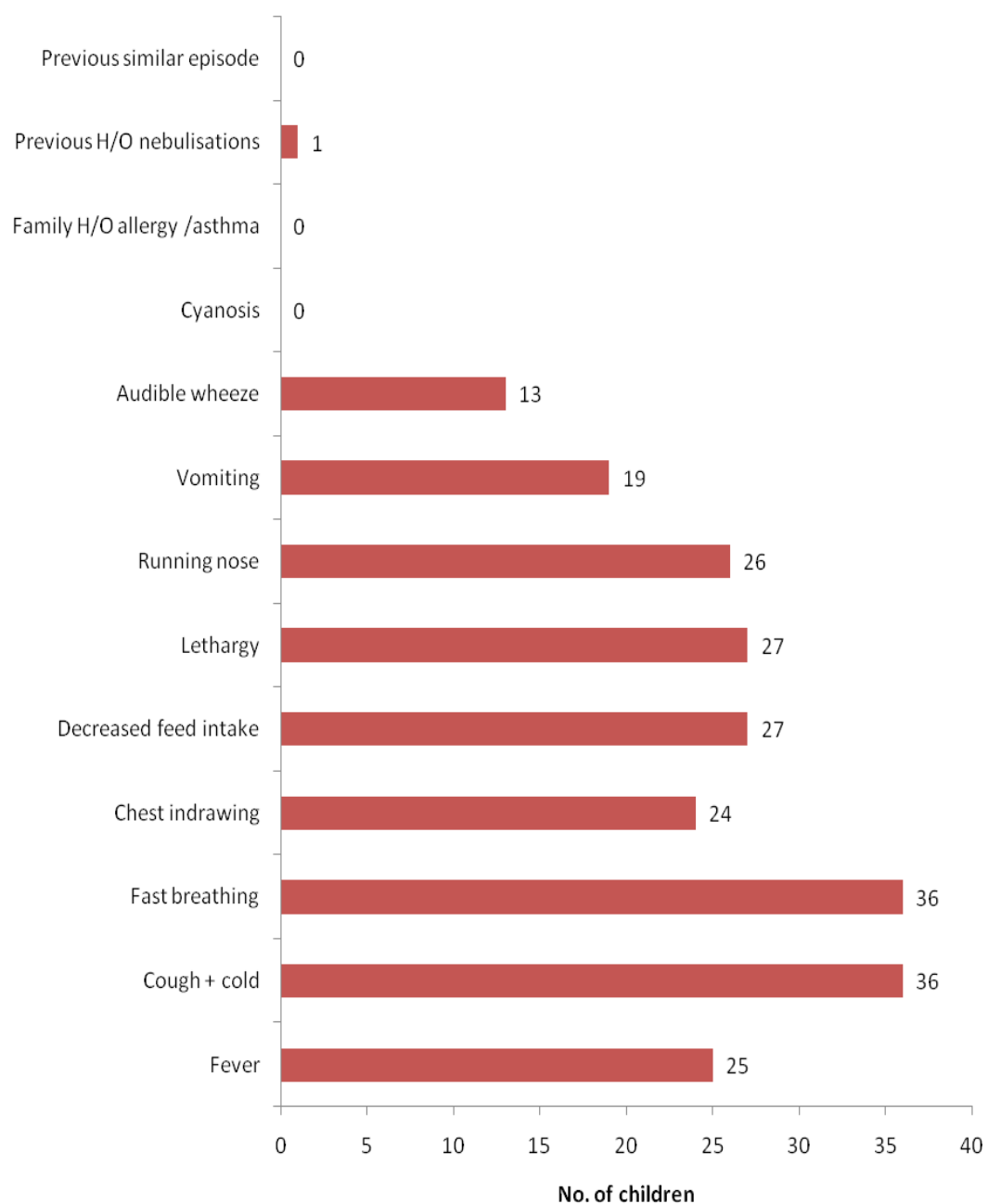


Table 3: Signs elicited in the 36 children

Signs	No. of children (n)	Percentage (%)
Temperature > 37.4°C	29	80.55
Undernutrition	31	86.11
Wheeze	1	2.77
Crepitations	35	97.22

Fig 2: Signs elicited in the 36 children

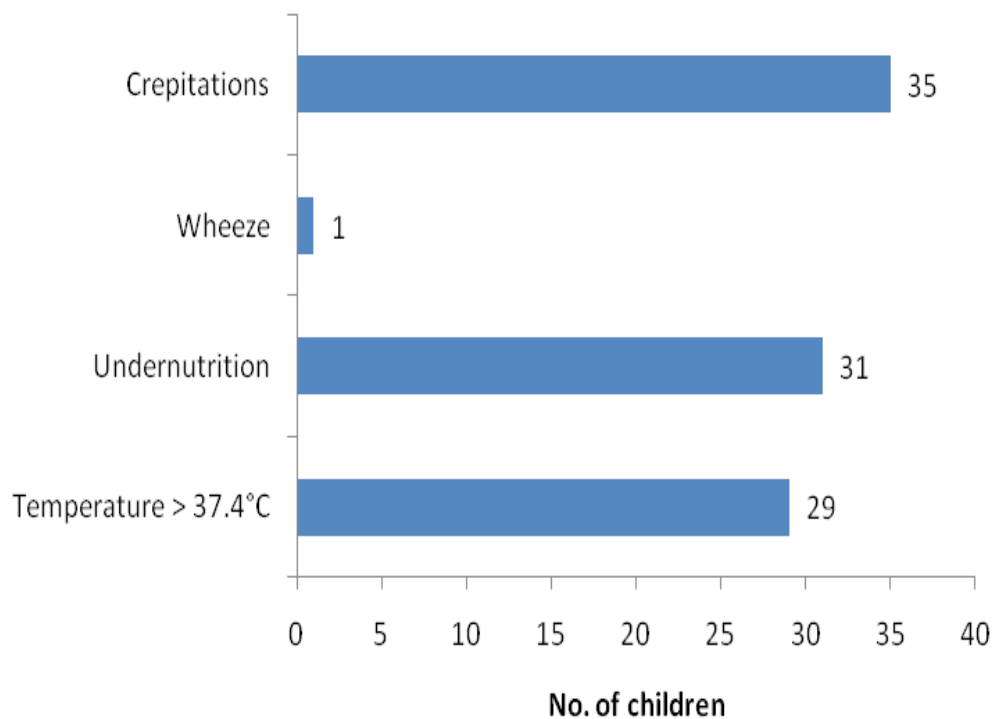


Table 4: Symptoms and History analysis of 205 children

Symptoms + History	No. of children (n)	Percentage (%)
Fever	97	47.31
Cough + cold	205	100
Fast breathing	205	100
Chest indrawing	82	40
Decreased feed intake	123	60
Lethargy	44	21.46
Running nose	52	25.36
Vomiting	37	18.04
Audible wheeze	30	14.63
Cyanosis	0	0
Family H/O allergy /asthma	47	22.92
Previous H/O nebulisations	80	30.92
Previous H/O respiratory distress	205	100
One episode	133	64.87
More than two episodes	72	35.12

Fig 3: Symptoms and history analysis of 205 children

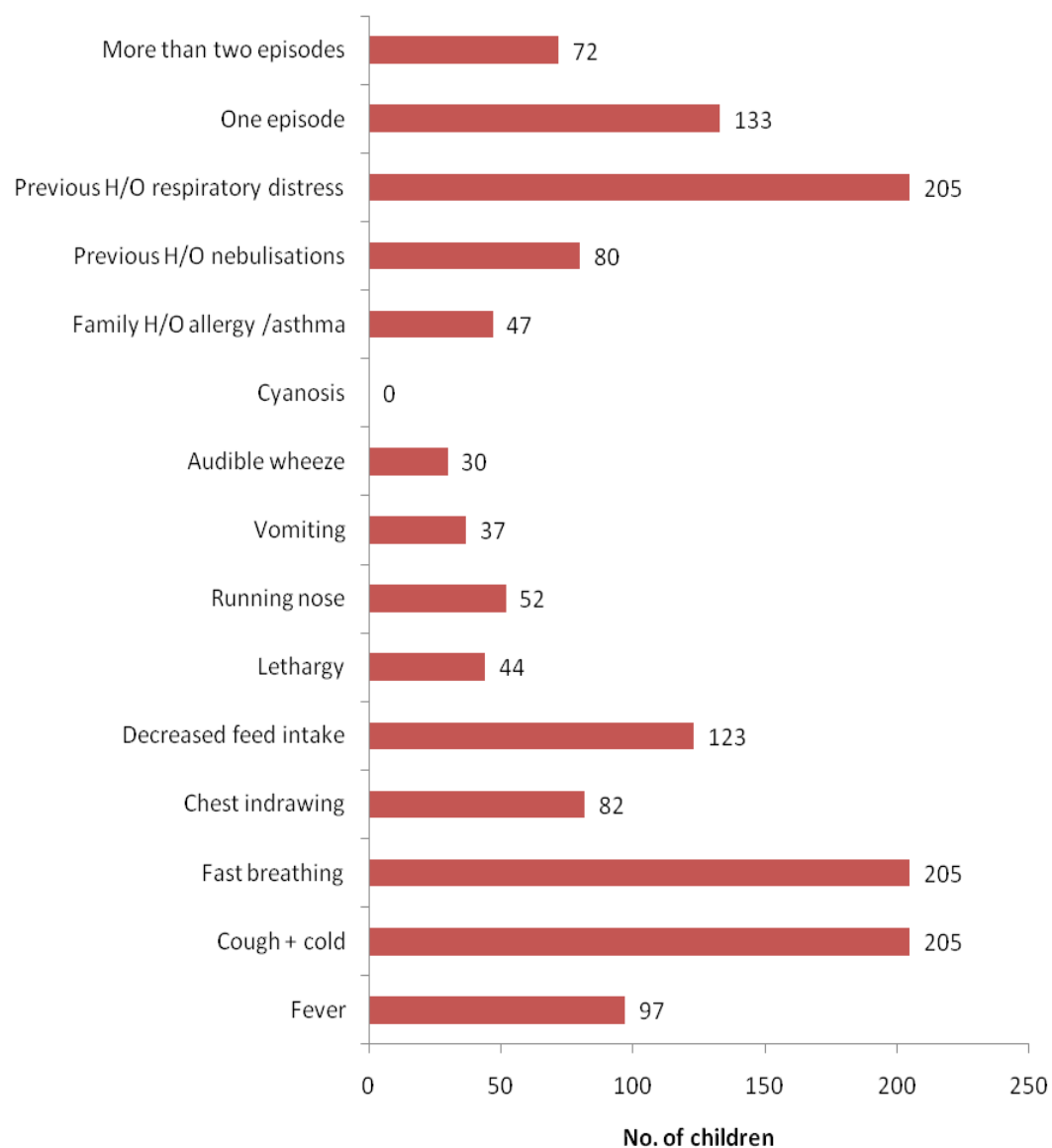
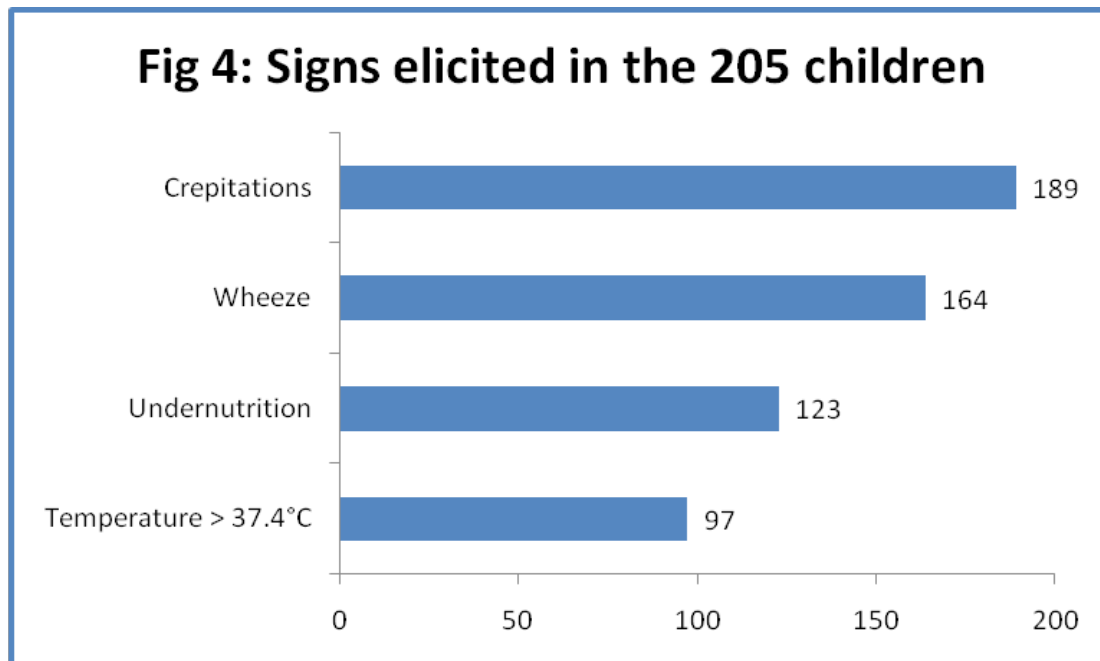


Table 5: Signs elicited in the 205 children

Signs	No. of children (n)	Percentage (%)
Temperature > 37.4°C	97	47.31
Undernutrition	123	60
Wheeze	164	80
Crepitations	189	92.19



205 children had a previous similar episode of cough and rapid breathing received bronchodilator challenge. The response of tachypnoea was then evaluated.

Table 6 : Association between persistence of tachypnoea after bronchodilator challenge and Pneumonia

Tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	56	14	70
No	20	115	135
Total	76	129	205

Sensitivity : 73.68% , Specificity : 89.14%, PPV : 80%, NPV : 85.18%

Among 76 children who had infiltrates radiologically, 56 children had persistent tachypnoea after trial bronchodilator. In 20 children tachypnoea disappeared (Sensitivity: 73.68). Out of 129 children who had no infiltrates on chest x ray 115 children showed resolution of tachypnoea following bronchodilator. But 14 children continued to have persistent tachypnoea despite normal chest x ray (Specificity: 89.14%). Out of 70 children with persistent tachypnoea, 56 children had infiltrates on chest x ray. (PPV = 80%). Out of 135 children whose tachypnoea resolved following bronchodilator, 115 children had normal x ray. (NPV = 85.18%). $p < 0.05$. Overall accuracy of persistent tachypnoea after bronchodilator in predicting pneumonia is 83.41%.

Table 7: Association between Fever and Pneumonia

Fever	X ray infiltrate		Total
	Yes	No	
Yes	60	37	97
No	16	92	108
Total	76	129	205

Sensitivity : 78.94% , Specificity : 71.31% , PPV : 61.85%,
NPV : 85.18%

Evaluating fever as a sign in predicting pneumonia against the gold standard of radiological infiltrate, 60 children who had fever had infiltrate in chest x ray. 16 children who did not have fever had infiltrate (Sensitivity: 78.94%). Out of 129 children who had normal x ray 92 did not have fever (Specificity: 71.31%). $p < 0.05$. Overall accuracy of fever in predicting pneumonia is 74.14%.

Table 8 : Association between Chest indrawing and Pneumonia

Chest indrawing	X ray infiltrate		Total
	Yes	No	
Yes	70	12	82
No	6	117	123
Total	76	129	205

Sensitivity : 92.10%, Specificity : 90.69%, PPV : 85.36%, NPV:95.12%

70/76 who had chest indrawing showed x ray infiltrate (Sensitivity: 92.10%). Out of 129 children with normal chest x ray, 117 children had no chest indrawing (Specificity : 90.69). 82 children with chest indrawing, 70 children had x ray infiltrates (PPV : 85.36%). Of the 123 children who did not have chest indrawing, 117 children had normal chest x ray (NPV : 95.12%). $p < 0.05$. The overall accuracy of chest indrawing in predicting pneumonia is 91.21%.

Table 9: Association between fever and persistence of tachypnoea and pneumonia

Fever + persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	53	17	70
No	23	112	135
Total	76	129	205

Sensitivity : 69.73% , Specificity : 86.82%, PPV : 75.71%, NPV:82.96%

53/70 children who had fever at presentation and showed no response of tachypnoea to bronchodilator had infiltrate on chest x ray (PPV : 75.71%). 23/135 children who had neither fever nor persistent tachypnoea following bronchodilator had infiltrate on chest x ray. On the other hand 17/70 children who had both fever and persistent tachypnoea after bronchodilator showed no infiltrate. 112/129 children were afebrile and tachypnoea disappeared after bronchodilator had normal chest x ray. (Specificity: 86.82%). $p < 0.05$. Accuracy of combined presence of both fever and persistent tachypnoea in predicting pneumonia is 80.48%.

Table 10: Association between chest indrawing and persistence of tachypnoea and pneumonia

Chest indrawing + persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	61	9	70
No	15	120	135
Total	76	129	205

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Sensitivity : 80.26%, Specificity : 93.02%, PPV : 87.14% , NPV:88.88%.

61/76 children who had both chest indrawing and persistent tachypnoea following bronchodilator had infiltrate on chest x ray (Sensitivity:80.26%) . 120/129 children who did not have chest indrawing and who showed good response to bronchodilator had normal chest skiagram(Specificity: 93.02%). $p < 0.05$. Accuracy of the combined presence of chest indrawing and persistent tachypnoea in predicting pneumonia is 88.29%

Table 11: Fever, chest indrawing and persistence of tachypnoea in combination, in predicting pneumonia

Fever + Chest indrawing + Persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	65	5	70
No	11	124	135
Total	76	129	205

Sensitivity : 85.52% , Specificity : 96.12% , PPV : 92.85% , NPV:91.85%.

65/76 children who had combined presence of fever, chest indrawing and persistent tachypnoea showed x ray infiltrates (Sensitivity : 85.52%). 124/129 children who did not have all the three characteristics had normal x ray (Specificity : 96.12%). 65/70 children who had infiltrates in x ray had fever, chest indrawing with persistence of tachypnoea in combination (PPV : 92.85%). Out of 135 children who had neither of these characteristics,124 children were with normal chest skiagram (NPV : 91.85%). $p < 0.05$. The combined presence of fever, chest indrawing and persistent tachypnoea following bronchodilator in predicting pneumonia has an excellent accuracy of 92.19% .

There were 72 children who had **either more than two previous similar episodes and/or family history of asthma and/or previous history of nebulisations**

- More than two similar episodes – 42.
- Family h/o asthma –13
- H/o previous nebulisations – 17

Presence of these factors either single or in combination may more likely suggest that ASTHMA may be the cause of cough and respiratory distress.

So we excluded these children and applied the same analysis in the rest (**n = 133**).

**Table 12: Association between persistence of tachypnoea after
bronchodilator challenge and pneumonia**

Tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	54	6	60
No	16	57	73
Total	70	63	133

Sensitivity : 77.14%, Specificity : 90.46%, PPV : 90.00%,
NPV : 78.08%

After excluding children who were more likely to be asthmatics, 54/70 children showed infiltrates on chest x ray had persistent tachypnoea. 16/70 children in whom tachypnoea resolved had infiltrates. (Sensitivity : 77.14%). 57/63 children in whom tachypnoea disappeared following bronchodilator had normal x ray. (Specificity : 90.46% an increase from 89.14%). $P < 0.05$.

Table 13: Association between fever and pneumonia

Fever	X ray infiltrate		Total
	Yes	No	
Yes	62	11	73
No	8	52	60
Total	70	63	133

Sensitivity : 88.57%, Specificity : 82.53%, PPV : 84.93%,
NPV : 86.66%

Sensitivity of fever in predicting pneumonia is 88.57%. On excluding the population of children in whom the cause of tachypnoea was likely to be asthma the specificity of fever in predicting pneumonia increased from 71.31% to 82.53%. $p < 0.05$.

Table 14 : Association between chest indrawing and pneumonia

Chest indrawing	X ray infiltrate		Total
	Yes	No	
Yes	65	5	70
No	5	58	63
Total	70	63	133

Sensitivity : 92.85%, Specificity : 92.06%, PPV : 92.85%,
NPV : 92.06%.

65/70 children, who had infiltrate presented with chest indrawing. 58/63 who did not have chest indrawing had normal chest x ray. Specificity has increased from 90.69% to 92.06% in these children.
 $P < 0.05$.

Table 15: Association between fever and persistence of tachypnoea and pneumonia

Fever+ persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	53	5	60
No	17	58	73
Total	70	63	133

Sensitivity : 75.71%, Specificity : 92.06%, PPV : 88.33% ,
NPV : 79.45%.

The combined presence of both fever and persistent tachypnoea in these children whose etiology for tachypnoea were more likely to be asthma has got a specificity of 92.06. There is an increase from 86.82% to 92.06% in these children when compared to the entire study population. $P < 0.05$

Table 16 : Association between chest indrawing and persistence of tachypnoea and pneumonia

Chest indrawing + persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	57	3	60
No	13	60	73
Total	70	63	133

Sensitivity : 81.42%, Specificity : 95.23%, PPV: 95%, NPV: 82.19%

The combined presence of both chest indrawing and Tachypnoea also showed increase in specificity from 93.02% to 95.23% in diagnosing pneumonia. $P < 0.05$.

Table 17: Association between fever, chest indrawing and persistence of tachypnoea and pneumonia

Fever + Chest indrawing + Persistent tachypnoea	X ray infiltrate		Total
	Yes	No	
Yes	58	2	60
No	12	61	73
Total	70	63	133

Sensitivity : 82.85%, Specificity : 96.82%, PPV : 96.66%,
NPV : 83.56%.

The simultaneous presence of fever, chest indrawing and persistent tachypnoea after bronchodilator in predicting pneumonia is highly specific for pneumonia. Specificity: 96.82% There is no significant increase in specificity in this study group when compared to the entire study population.

TABLE 18:

Association of pneumonia with the following	Sensitivity (%)		Specificity (%)	
	n1= 205	n2= 133	n1= 205	n2= 133
Persistent tachypnoea	73.68	77.14	89.14	90.46
Fever	78.94	88.57	71.31	82.53
Chest indrawing	92.10	92.85	90.69	92.06
Fever + Persistent tachypnoea	69.73	75.71	86.82	92.06
Chest indrawing + Persistent tachypnoea	80.26	81.42	93.02	95.23
Fever + Chest indrawing + Persistent tachypnoea	85.52	82.85	96.12	96.82

n1: Entire study population

n2: excluding likely asthmatics

FOLLOW UP

On follow up of 115 children who were sent home with bronchodilator after two days, only 47 children came for follow up (40.86%). Of these 47 children 39 were normal, 5 children had another acute attack. They were treated with bronchodilator. 3 children who initially had fever and chest indrawing got deteriorated and hence were admitted.

DISCUSSION

At the time of conception of case management of WHO guidelines for case management of childhood pneumonia in early eighties, pneumonia was assumed to be the predominant condition presenting with cough, cold and fast breathing^{1,2}. Upto this time enough data has been accumulated to highlight the increasing prevalence and severity of asthma globally^{11,13,14}. There is a considerable overlap in clinical presentation of pneumonia and asthma. It is also important to emphasise that asthma related fatalities do occur^{20,21} and can be effectively prevented by accurate diagnosis and early institution of treatment with bronchodilators.

WHO-IMNCI case management of ARI was developed in order to assist the field workers to reliably identify children with ARI and to institute treatment. It also enables them identify those children who need to be immediately referred to hospital^{2,8}. It has also been advocated to treat the children presenting with recurrent wheeze (audible) with trial of bronchodilators^{15,26}.

Further, the need for bronchodilator therapy is guided by the presence of a wheeze which for paramedical personnel pertains to only an estimated one-third episodes in which the wheeze may be audible without the aid of a stethoscope²⁶.

Thus, according to the current guidelines, in a child with cough and rapid breathing, there is a predilection for over-treatment for pneumonia with antibiotics and for under-treatment for asthma with broncho-dilators^{22,23,25}.

In this study, there were 205 children between 6 months to 59 months age group presented with acute cough and respiratory distress with previous history of similar episode. These children received trial nebulisations with careful monitoring. The response of tachypnoea to nebulisations was then assessed. 135/205 children showed good response to nebulisations and their tachypnoea resolved. 115/135 children had a normal chest skiagram (NPV: 89.14%). Fever, defined as temperature of $>37.4^{\circ}\text{C}$, has specificity of 71.31% in predicting pneumonia. Chest indrawing had an excellent specificity of 90.69%. However the combined presence of fever, chest indrawing and persistent tachypnoea in predicting the presence of infiltrates on chest x ray has a very high sensitivity of 85.52% and specificity of 96.12%.

There were 72 children, who either had more than two similar episodes and/or family H/O asthma and/or previous H/O nebulisations; in these children acute cough and respiratory distress may have been due to asthma. Excluding these 72 children the same analysis was done in the rest 133 children. As expected the specificities of fever, chest indrawing and persistent tachypnoea either alone or in combination showed an increase from the entire study population indicating the clinical picture could have been due to asthma.

In short, pneumonia (presence of infiltrates on chest x ray) was diagnosed only in 76/205 children (37.07%) which is in accordance with the great importance of asthma as a cause of respiratory distress.

There are similar such studies which also found a low prevalence of pneumonia in children presenting with cough and rapid breathing. Study conducted by A.V Castro

et al in Brazil²⁵ showed that pneumonia was radiologically diagnosed in only 15.8% of the children who presented with cough and rapid breathing. Another study conducted by H.P.S. Sachdev et al ^{22,23} in New Delhi also showed only 10% of x ray showing infiltrate in similar children.

This study demonstrated association between persistent tachypnoea after bronchodilator in children with previous H/O respiratory distress and presence of pulmonary infiltrate ($p = 0.0001$). By employing this algorithm, 85.18% of children did not receive unnecessary antibiotics.

This is in accordance with the study conducted by A.V. Castro et al where the NPV of resolution of tachypnoea after trial with bronchodilator was 87.3%²⁵. The response to bronchodilator in children with previous history of respiratory distress could reduce the use of antibiotics in regions where there is an increasing prevalence of asthma. This would also prevent the problem of development of antimicrobial resistance by unnecessary use of antibiotics^{6,29,30}.

Presence of fever at the onset, has a good specificity in diagnosis of pneumonia. This is not in accordance with the study by A.V.Castro which showed no significant association between fever and pneumonia²⁵. But our Indian study conducted in New Delhi in 1995 showed absence of fever is associated with asthma rather pneumonia²².

The presence of chest indrawing is significantly associated with pneumonia ,with a very high specificity of 90.69%. This is not in accordance with the result of the study conducted in Brazil by A.V. Castro²⁵ where the presence of chest indrawing has a poor

correlation with pneumonia. The presence of fever, chest indrawing and persistent tachypnoea has a significant association with the presence of infiltrate in chest x ray with the highest specificity of 96.12%.

On excluding 72 children who either had previous H/O nebulisations and/or family H/O asthma, and/or more than two episodes in whom asthma may be a cause of cough and respiratory distress the specificity of fever, chest indrawing, persistent tachypnoea either alone or in combination in diagnosis of pneumonia (presence of infiltrate) increased.

This is in accordance with the result of the study conducted by H.P.S Sachdev 1994 which showed that the best predictor for asthma was two or more earlier similar episodes (sensitivity 84%, specificity 84%) followed by temperature $<37.6^{\circ}\text{C}$ (sensitivity 73% and specificity 84%). Absence of fever, audible wheeze and a family history of asthma had excellent specificities (98-100%) but low sensitivities (20-34%). It is concluded that these simple clinical predictors can differentiate acute asthma and ARI^{22,23}.

SUMMARY

To summarize the results of the study,

- The combination of fever, chest indrawing and persistent tachypnoea after bronchodilator has an excellent specificity of 96.12% in predicting the presence of pulmonary infiltrate
- Correction of tachypnoea after bronchodilator therapy has a good negative predictive value of 85.18% in the diagnosis of pneumonia.
- The presence of more than two episodes of similar respiratory distress, previous H/O of nebulisations and family H/O asthma, either alone or in combination may point more towards asthma as a cause of cough and respiratory distress.

CONCLUSION

- In a child presenting with cough and fast breathing with a previous similar episode, trial nebulisations can be given before investigating further for pneumonia.

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ANNEXURE

DATA ENTRY FORM

Serial No:

Name:

Age:

Weight:

Sex:

Father's name:

Address:

Complaints:

H/O previous similar episodes:

H/O antibiotic use:

Foreign body aspiration:

Lethargy:

Decreased activity:

Decreased intake of feeds:

Convulsions:

Audible wheeze:

H/O bluish discoloration
of tongue and nail bed:

H/O altered sensorium:

H/O of vomiting and/ loose stools:

H/O decreased urine output:

Known case of asthma:

Family H/O asthma and/ allergy:

H/O other chronic illness:

Examination

Nutritional status:

Hydration status:

Temperature:

Respiratory system:

Respiratory rate:

Chest indrawing:

Nasal flaring:

Grunt:

Cyanosis:

Stridor

Audible wheeze:

Air entry:

Added sounds:

Cardiovascular system:

Apex:

Heart sounds:

Murmur:

Abdomen:

Organomegaly:

Central nervous system:

Higher function:

Pupils:

Focal deficit:

Bronchodilator	Cough	Respiratory rate	Chest indrawing

Chest X ray:

Advice:

Follow up: